

**Title:** Can genetic testing predict talent? A case study of five elite athletes.

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**Authors:** Craig Pickering<sup>1</sup>, John Kiely<sup>1</sup>

1. Institute of Coaching and Performance, School of Sport and Wellbeing, University of Central Lancashire, Preston, UK

Corresponding Author:

Craig Pickering

Institute of Coaching and Performance, School of Sport and Wellbeing, University of Central Lancashire, Fylde Road, Preston, PR1 2HE, UK.

Email: [craigpickering1014@hotmail.com](mailto:craigpickering1014@hotmail.com).

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## Can genetic testing predict talent? A case study of five elite athletes

### Abstract

**Purpose:** The genetic influence on the attainment of elite athlete status is well-established, with a number of polymorphisms found to be more common in elite athletes than in the general population. As such, there is considerable interest in understanding whether this information can be utilised to identify future elite athletes. Accordingly, the aim of this study was to compare the total genotype scores of five elite athletes to those of non-athletic controls, to subsequently determine whether genetic information could discriminate between these groups, and, finally, to suggest how these findings may inform debates relating to the potential for genotyping to be used as a talent identification tool. **Methods:** We compared the total genotype scores for both endurance (68 genetic variants) and speed-power (48 genetic variants) elite athlete status of five elite track and field athletes, including an Olympic Champion, to those of 503 Caucasian non-athletic controls. **Results:** Using the speed-power total genotype score, the elite speed-power athletes scored more highly than the elite endurance athletes. However, using this speed-power score, 68 non-athletic controls registered higher scores than the elite power athletes. Surprisingly, using the endurance total genotype score, the elite speed-power athletes again scored more highly than the elite endurance athletes. **Conclusions:** These results suggest that genetic information is not capable of accurately discriminating between elite athletes and non-athletic controls, illustrating that the use of such information as a talent identification tool is currently unwarranted and ineffective.

### Key words:

Genetic testing; elite athlete; talent; talent identification; Olympic

## Introduction

Over the last thirty years, our appreciation of how genetics influences elite sports performance has grown exponentially, with previous estimates of the heritability of elite athlete status within a population reported to be approximately 66%.<sup>1</sup> Similarly, our understanding of how specific genetic variants, such as *ACTN3*,<sup>2</sup> may predispose towards elite performance has developed. Such advances have led to speculation that genetic testing may be a viable tool to identify individuals with an increased likelihood of achieving elite athlete status in the future, with some direct-to-consumer genetic testing companies already offering this service.<sup>3</sup>

However, at present, the scientific consensus suggests that such approaches are ineffective at identifying future talented performers.<sup>3</sup> Previously, Williams & Folland<sup>4</sup> incorporated 23 genetic variants associated with elite endurance performance in a data simulation, with subsequent results suggesting that there was only a 0.0005% chance of any single person in the world having the optimal form of all 23 performance-associated variants. A further issue is that, within this simulation, there was considerable similarity in polygenic profiles between individuals, with the clustered distribution of genotype scores limiting the emergence of genetic outliers, who we might reasonably predict are more likely to be elite athletes. Similar findings, relating to muscular strength and power characteristics, have also been demonstrated.<sup>5</sup> Such issues have also been explored experimentally, most commonly via the use of Total Genotype Scores (TGS). Here, a score is assigned for each genotype of interest, and then summed into a final score for that athlete. For example, Ruiz and colleagues<sup>6</sup> collected data on elite Spanish endurance athletes and controls. Whilst, on average, the athletes within that cohort had a greater TGS for a panel of seven endurance-related polymorphisms than non-athletic controls, there was considerable overlap in score between the populations, thereby illustrating that the predictive capability of this particular TGS was low. Indeed, whilst individuals with a TGS above 74.71 were over five times more likely to be elite athletes, only 43.5% of elite athletes attained such a score. Similar results were reported for elite power athletes;<sup>7</sup> again, the athletes had a higher average power TGS than both controls and endurance athletes, but with a large crossover of standard deviations between the groups, indicating limited sensitivity and specificity.

Such evidence suggests that utilising a relatively low number of polymorphisms to identify elite athletes is unlikely to provide meaningful insights. However, many more polymorphisms than the 23 or fewer utilised in the studies to date have been associated with elite performance. A recent literature review,<sup>8</sup> for example, reported that at least 155 genetic markers have been associated with elite athlete status, with further associations emerging since that article's publication.<sup>9</sup> Additionally, in a recent survey in the UK, 67% of athletes and 48% of support staff stated that genetic testing would form a valuable addition to talent identification processes within their sport,<sup>10</sup> suggesting that there is an appetite for such information within the sports performance world.

Despite this apparent enthusiasm, however, further research in this area is clearly required. Currently, it remains unclear whether genetic information can accurately discriminate between elite performers and members of the general public. In addressing this lack of evidence-led insight, within this investigation we used an expanded TGS, incorporating an increased number of genetic variants, to determine whether such a panel can reliably distinguish between a sub-population of five elite athletes and a control population of European Caucasians. To the best of our knowledge, such a large scale TGS has not

previously been utilised to identify talented athletes, demonstrating the novelty of such a case study.

## **Methods**

### **Participants**

The participants were five former or current high-level athletes. All participants gave written, informed consent for their genotype results and identity to be shared here. All participants read the final version of this manuscript prior to submission, and consented to its publication, and their naming within this publication. The study protocol was approved by the University of Central Lancashire Ethics Committee, in accordance with the Declaration of Helsinki (Ethics Board number BAHSS 575)

Participant A (Andrew Steele) is a former 400m runner. He competed at one Olympic Games, winning a medal in the 4x400m relay. His personal best time is 44.94s, and he was a high-level athlete for approximately 11 years.

Participant B (Greg Rutherford) is a former long jumper. He has competed at three Olympic Games, winning a Gold and a Bronze medal. His personal best distance is 8.51m, and he was a high-level athlete for approximately 13 years.

Participant C (Craig Pickering) is a former sprinter. He competed at one Olympic Games, and has a World Championships Bronze medal in the 4x100m relay. His personal best 100m time is 10.14s, and he was a high-level athlete for approximately 7 years.

Participant D (Tom Lancashire) is a middle-distance runner, competing primarily over 1500m, the distance at which he was selected for an Olympic Games. His personal best 1500m time is 3:33:96, and he was a high-level athlete for approximately 13 years.

Participant E (Andrew Lemoncello) is a long-distance runner, with a Marathon personal best time of 2:13:40. He competed at two World Championships, and one Olympic Games, and was a high-level athlete for approximately 12 years.

All participants are of primarily European Caucasian ethnicity, although Participant D's mother is Mauritian.

### **Genetic Testing**

Each participant volunteered a saliva sample, which was collected through sterile and self-administered buccal swabs. The samples were sent to AKESOGen, Inc (Peachtree Corners, GA, USA), where DNA was extracted from the saliva samples using Qiagen chemistry on an automated Kingfisher FLEX instrument (Thermo Fisher Scientific, Waltham, MA, US), following the manufacturer's recommended protocols and standard operating procedures. PicoGreen and Nanodrop measurements were taken to measure the quality and quantity of the DNA. Input to the custom testing array occurred at 200ng in 20µL. Amplification, fragmentation, and resuspension was performed using Biomek FXP following Affymetrix's high throughput protocol for Axiom 2.0. Hybridization was performed for 24 hours at 48°C in a Binder oven, and staining and scanning of the arrays was performed using GeneTitan instrumentation (Thermo Fisher Scientific, Waltham, MA, US), all following the same Affymetrix high throughput Axiom 2.0 protocol. Data analysis was

then performed using a raw CEL file data input into the Affymetrix Axiom Analysis Suite (Affymetrix, Santa Clara, CA, US).

### Creation of Total Genotype Scores

In order to best examine the potential use of genetic information in identifying elite athletes, polymorphisms previously linked to elite speed-power and elite endurance athlete status were collated through a structured literature search.

*Speed-Power Athlete Status:* A total of 48 genetic variants associated with power athlete status were identified from two review articles.<sup>8,11</sup> Of these 48, one marker (*IL1RN*) could not be genotyped due to lack of coverage on the AKESOgen chip array. A further SNP, rs2854464 in *ACVR1B*, was added to the panel based on subsequent research.<sup>12</sup> Three additional SNPs in the carnosine genes *CNDP1* and *CNDP2*, associated with elite power athlete status<sup>9</sup> were also not present on the chip array, and so were not assessed. Mitochondrial DNA (mtDNA) was not assessed. The effect allele of one SNP, rs11091046 in *AGTR2*, was reversed given the findings of a recent meta-analysis.<sup>13</sup> Accordingly, 48 genetic variants were utilised in the power TGS within this study.

*Endurance Athlete Status:* A total of 68 genetic variants associated with endurance athlete status were identified from two review articles.<sup>8,11</sup> Of these, the genotype of 5 (*ADARA2A* 6.7/6,3kb, *BDKRB2* +9/-9, *COL5A1* rs71746744, *NOS3* 4A/4B, *PPP3R1* 5I/5D) could not be determined due to insufficient coverage. We also added rs10497520 *TTN* to the TGS.<sup>14</sup> mtDNA was not assessed. Accordingly, 64 genetic variants were utilised in the endurance TGS within this study.

### Scoring

For each genetic variant, a score of 0, 1 or 2 was given depending on the genotype of the athlete. A score of 2 represents the possession of two alleles associated with elite athlete status (e.g. CC for *ACTN3* rs1815739 within the power TGS); a score of 1 represents carriage of one such allele (e.g. CT for *ACTN3* rs1815739 within the power TGS); and a score of 0 represents the possession of no elite athlete-associated alleles for that genetic variant (e.g. TT for *ACTN3* rs1815739 within the power TGS). For each trait, the scores were then summated, divided by the total possible score, and multiplied by 100 to get a percentage. This method is identical to that utilised in previously published research utilising a TGS to explore elite athlete status.<sup>4-7</sup> The analysis was carried out in Excel 16.13.1 (Microsoft, Redmond, WA, USA).

### Control Population

In order to develop an adequate control population, genotype scores for 503 European Caucasians were downloaded from e!GRCh37 (<http://grch37.ensembl.org/index.html>) into a spreadsheet for analysis. For each genetic variant, a score of 0, 1, or 2 was given as per the speed-power and endurance TGS detailed previously. The sum of scores for each variant was then calculated, and converted into the TGS% as per the previously detailed method. Additionally, the mean and standard deviation score for this reference population were calculated.

### Results

#### TGS Scores

Table 1 shows the results of all five participants' speed-power TGS, as well as the mean score expected in European Caucasians. The three speed-power athletes had the highest TGS, whilst the two endurance athletes had the lowest. This trend held up in comparison to the mean score for European Caucasians, with the speed-power athletes having a higher score than the mean, and the endurance athletes a lower score than the mean. Table 1 also demonstrates the results of the endurance TGS. Here, the two endurance athletes still have the lowest TGS – lower than the elite speed-power athletes and the mean for European Caucasians.

**Insert Table 1 around here**

### **Comparison to previously published TGS**

The next stage of our analysis was to calculate the TGS from previously published research by Ruiz and colleagues.<sup>6,7</sup> The results for both the speed-power and endurance TGS developed by Ruiz are shown in table 2.

**Insert Table 2 around here**

### **Non-athlete Control Results**

We then calculated the frequency distributions for 503 non-athletic Caucasian controls for both the power (figure 1) and endurance (figure 2) TGS. In general, the results of the controls are fairly tightly distributed around the mean. Within the power TGS, no participants fell below a score of 26%, or above a score of 53%. Similarly, within the endurance TGS, no participant had a score below 34% or above 55%.

**Insert Fig 1 around here**

**Insert Fig 2 around here**

### **Discussion**

Using a 48 SNP TGS of speed-power associated SNPs, we found a general trend for the elite speed-power athletes to score more highly (range 42.7-44.8%) than the elite endurance athletes (37.5%) in our cohort. The mean score for our control population of European Caucasians was 39.4%; lower than the scores achieved by the speed-power athletes, but higher than the elite endurance athletes. These outcomes may appear to provisionally support the use of genetic information to identify talented performers; however, both endurance athletes and two of the three power athletes were within one standard deviation of the non-athletes mean score. Indeed, in the 503 European reference samples utilised, 68 individuals had higher speed-power TGSs than athlete A, the highest scoring athlete in our cohort. The highest score in the control population was a TGS of 50%, just over 2SDs greater than the mean.

The results for the 64 SNP endurance TGS further demonstrated the lack of utility of genetic testing for talent identification. Here, all three speed-power athletes (range – 43.8-47.7%) out-scored the endurance athletes (39.8 – 42.2%), who in turn scored lower than the

mean for European Caucasians (43.8%). The SD for scores in the 503 European reference samples was 3.8%, with 82 control participants having an endurance score >1SD outside of the mean. The highest score was 54.6%.

The comparison to the previously published TGS utilised by Ruiz and colleagues<sup>6,7</sup> provides some interesting results. In our cohort, the elite endurance athletes scored more highly on Ruiz and colleagues' <sup>6</sup> endurance TGS (64 and 71%) than our speed-power athletes. This is the opposite result to that seen when utilising the larger scale TGS developed for our study. This potentially suggests that the utilisation of fewer genetic variants within a TGS may enhance the predictive ability of such a model, potentially because the selected variants have a greater effect size, or that the reported effects in the literature are correct, and not spurious. Larger sample sizes are required to further test this. Regarding the power TGS, the athletes in our cohort all scored lower than the mean power score in the Ruiz and colleagues<sup>7</sup> cohort; two just outscored the mean for European Caucasians, whilst participant C—a European medalist over the 60m sprint—scored below the mean for European Caucasians, and was outscored by participant E, the long-distance runner. Again, this is in contrast to our results, where the speed-power athletes all outscored the endurance athletes, suggesting that the larger scale TGS is potentially more sensitive in determining speed-power athlete status.

The two genetic variants most well-associated with elite athlete status are *ACE* and *ACTN3*.<sup>2,15,16</sup> Regarding *ACTN3*, the C allele of rs1815739 is consistently associated with elite speed-power athlete status, with two recent meta-analyses<sup>17,18</sup> finding that individuals with the TT genotype were significantly less likely to achieve elite speed-power athlete status compared to those with at least one C allele. The three speed-power athletes within our cohort exhibit the full range of *ACTN3* genotypes (data not shown). Participant B, the highest achieving of our cohort, possesses the CC genotype. Participant C, the short sprinter, possesses the CT genotype, whilst Participant A, the Olympic 400m relay medallist, is a TT genotype. This latter result is somewhat surprising given that this genotype is considered unfavourable for elite speed performance, a result which has also been demonstrated in 400m runners.<sup>16</sup> Furthermore, the endurance athletes in this cohort possessed the CT and CC genotype respectively, both of which might be considered slightly unfavourable for elite endurance performance.<sup>17</sup> This relationship, however, appears complex and poorly understood; whilst some studies suggest an association between the *ACTN3* T allele and elite endurance status<sup>2</sup>, others do not.<sup>19</sup>

The genotype results for *ACE* were similarly heterogenous (data not shown). For this genetic variant, the D allele is considered favourable for elite speed-power athlete status,<sup>17,18</sup> with the I allele favourable for elite endurance athlete status.<sup>17</sup> Within our speed-power cohort, two athletes had the ID genotype, and one the II genotype; neither is considered optimal for elite speed performance. Conversely, both endurance athletes had the favourable II genotype.

Non-athletic controls exhibited extensive similarities in polygenic profiles, with a minimal spread of results across individuals. This similarity in polygenic profiles in non-athletes has previously been reported with a lower number of generic variants for both endurance<sup>4</sup> and strength/power<sup>5</sup> phenotypes. Within this case study, none of the elite athletes were significant outliers in terms of TGS%, demonstrating that, for the polymorphisms tested, genetic information is not sufficient to discriminate between elite athletes and non-athletic controls.

## **Would genetic testing have helped identify these athletes at a young age?**

Based on these results, it seems unlikely that genetic testing of these athletes during their teenage years would have correctly identified them as potential future elite athletes relative to a group of non-athletes. In fact, it's unlikely that this information would have proved more useful than traditional talent identification methods. Participant A, for example, was English Schools 400m Champion at age 16. Participant B is the British under-20 Long Jump record holder and former European under-20 Champion. Participant C won multiple national age group titles at under-15 and under-17, and the European under-20 Championships. Participant D won multiple junior national titles, and Participant E also won national age-group championships. Consequently, given the failure of genetic information to provide insights over and above that provided by inspecting results and observing performances, the practical utility of such tests for the specific purpose of talent identification is not supported by these case study results. In addition, the utilisation of genetic testing in under-18s is ethically troubling, with a number of key researchers recommending against such practice.<sup>3,20,21</sup>

## **Limitations**

There are some limitations to the present study that must be considered when interpreting the results. Firstly, we were unable to collect data on mitochondrial DNA (mtDNA). Mitochondrial haplotypes have been associated with elite athlete status, with different variations conferring an advantage or disadvantage in achieving elite athlete status for both speed-power and endurance athletes.<sup>8,22-24</sup> Furthermore, we were unable to collect genotype data for a small number of polymorphisms, due to a lack of coverage on the testing array. There is the potential that the athletes in this study may have held favorable versions of these variants, which would have increased their scores. Nevertheless, even given these limitations, the genotype panel created for use in this study represents the most comprehensive gene score to appear in the published literature with regards to elite athlete status. Furthermore, we utilised an unweighted TGS, with each variant having a score of 0, 1, or 2 depending on genotype. A weighted TGS, with genetic variants with demonstrably larger effect sizes getting a greater score, may have proved more accurate. However, at present, very few genetic variants associated with elite athlete status have been adequately replicated, making the development of such a weighted, multi-variant TGS difficult to achieve.

In addition, the comparison population utilised within this study was an anonymous group of 503 European Caucasians. One issue with using such a group is that the identities of the participants is unknown; there is the possibility that this group was comprised of a large number of elite athletes, which would have skewed the results, although this is very unlikely. Finally, the sample sized utilised within this study is extremely limited, with further research with larger numbers of athletes required.

## **Practical Applications**

It seems clear that, at present, genetic testing cannot adequately discriminate between elite athletes and non-athletes. In the current study, the TGS scores of five elite athletes did not deviate substantially from average population scores, nor did they reach the thresholds typically seen in elite athletes from other published TGS-elite athlete status associations,<sup>6,7</sup> although the number of genetic variants used within these earlier studies was very small. Indeed, within this present cohort, and utilising a larger-scale TGS, all three of the elite power athletes had a higher endurance score than both the middle-distance and long-distance



runners. As a result, it appears that current commercially available genetic tests purporting to assist in the talent identification process have minimal utility,<sup>21</sup> and should not be used.<sup>3</sup>

Athletic success is predicated on a wide variety of capacities. In the future, as a greater number of genetic variants associated with elite athlete status are identified, especially in areas involved in the psychological,<sup>25,26</sup> anatomical,<sup>27</sup> and skill acquisition<sup>28</sup> aspects associated with elite athlete status, it is feasible that the predictive ability of future TGSs may improve. Such improvements could be further facilitated by the use of weighted algorithms, where genetic variants with relatively larger effect sizes achieve a higher relative score compared to variants with a smaller effect size. However, at present, and as clearly illustrated by this case study involving highly elite athletes, the similarity of polygenic profiles within populations limits the capacity of genetic information to adequately discriminate between the general population and high performing athletes. For further insights into the limitations of genetic testing for talent identification, interested readers are directed to reviews by Webborn and colleagues<sup>3</sup> and Pickering et al.<sup>21</sup>

## Conclusion

The results of this study suggest that, at present, the ability to utilise genetic information to identify talented performers holds limited predictive utility. The reasons for this are potentially varied, but include a limited understanding of the genetic variants that predispose to elite performance, the importance of non-genetic factors in the talent development process, and a similarity of polygenic profiles amongst athletes and controls.

## Footnotes

**Supplementary files:** S1 – List of SNPs included within the TGS utilised within this study.

**Funding:** Genetic testing for this case study was provided free of charge by DNAFit Life Sciences, a genetic testing company.

**Competing interests:** CP is a former employee of DNAFit Life Sciences, a genetic testing company. He received no payment for carrying out this work, which was undertaken as part of his doctoral studies. JK has no competing interests relevant to the content of this article to declare. The results of the current study do not constitute endorsement of the product by the authors or the journal.

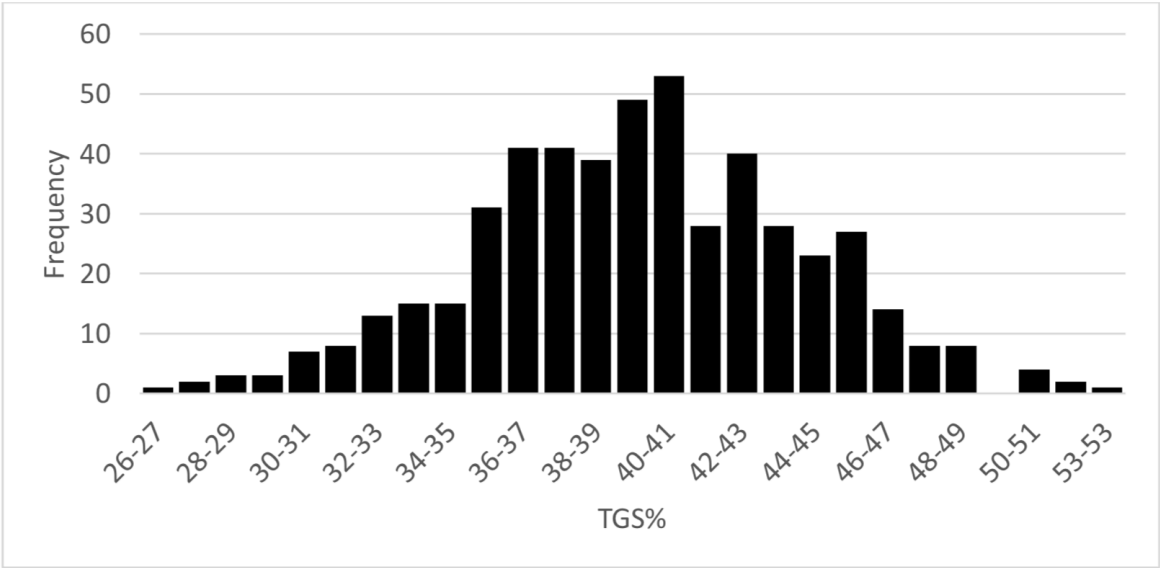
**Data availability:** Athlete genotype data, other than that reported here, cannot be shared due to the terms of the ethics approval. Genotypes of the non-athletic controls are publicly available.

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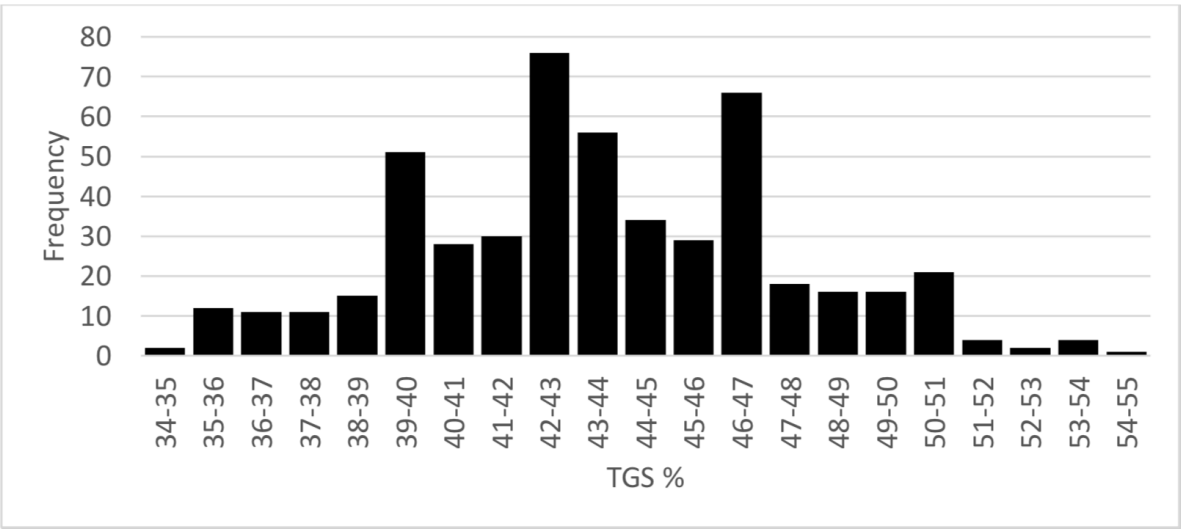
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Figure Captions



**Fig. 1** Frequency distribution of power TGS% for non-athletic controls



**Fig. 2** Frequency distribution of endurance TGS% for non-athletic controls

<b>Participant</b>	<b>A</b>	<b>B</b>	<b>C</b>	<b>D</b>	<b>E</b>	<b>European Average</b>
<b>Speed TGS</b>	44.8	43.8	42.7	37.5	37.5	39.4
<b>Endurance TGS</b>	46.9	47.7	43.8	42.2	39.8	43.8

Table 1 – Comparison of athletes’ scores in both the speed and endurance TGS utilised within this study, against the European Average score.

<b>Participant</b>	<b>A</b>	<b>B</b>	<b>C</b>	<b>D</b>	<b>E</b>	<b>European Average</b>	<b>Ruiz Endurance</b>	<b>Ruiz Power</b>
<b>Ruiz Power TGS<sup>7</sup></b>	66.7	66.7	50	50	58.3	62.5	60	70
<b>Ruiz Endurance TGS<sup>6</sup></b>	57.1	42.9	57.1	64.3	71.4	60.7	70.2	

Table 2 – Overview of the athletes’ scores on previously published research by Ruiz and colleagues<sup>6,7</sup>.